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Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Re: PhRMA Comments on Draft Guidance for Industry on Information Program on Clinical Trials for Serious or Life-Threatening Diseases: Establishment of a Data Bank
Docket No. 00D-1033, 65 Fed. Reg. 16620 (March 29, 2000)

Dear FDA:

On behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA) we are providing comments on the above-referenced draft guidance that was published in the March 29, 2000 issue of the *Federal Register*. PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer, healthier and more productive lives. Investing over $26 billion this year in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures. These companies are the source of nearly all new drugs that are discovered and marketed throughout the world.

As stated in our April 28, 1998 comments to NIH and FDA, we feel the public health can benefit from giving patients increased access to clinical trials. Such increased access hopefully will result in more patients enrolling in investigational drug trials, more efficient development of new and innovative therapies and ultimately more options and improved quality of life for patients. At the same time, care must be taken to ensure that the information disseminated to the public is of a rigorous nature (relevant, timely and accurate, as well as useful and beneficial to patients), and that any program that facilitates increased access neither compromises sponsor data that is proprietary (and should not be required to be reported in the data bank), nor creates administrative burdens that delay the drug development process.

Note: The following comments are organized by relevant section heading from the FDA draft guidance (i.e., comments below address sections I, III, and VI of the draft guidance):

00D-1033 C2

I. Introduction

The *Federal Register* notice indicated that later this year additional guidance will be published for comment, consisting of an implementation plan setting forth the logistics of providing and maintaining accurate and timely data in the data bank. When that later guidance is proposed, we urge that it include provision for phase-in of compliance requirements, including a reasonable future compliance date after which new trials should begin to be reported. The guidance should also address the issue of trials in progress after the compliance date. During start-up of the data bank there will be trials in progress where enrollment is complete or nearly complete, and by the time the information is first nominally required to be reported to the data bank the study will be closed to further patient entry. Requiring the inclusion of such trials retrospectively would only serve to add to the reporting burden by sponsors, without serving the patient needs intended to be addressed by Congress in the data bank.

III. Statutory Requirements for IND Sponsors

A. Data Requirements

The descriptive information collected on a clinical trial should meet FDAMA's requirement to be "readily understood by members of the public." Therefore, the "reformatting" of descriptive data that is provided to FDA under 21 CFR Part 312 for submission into the Clinical Trials Data Bank should be stated in language that is easily understood by the public. Technical information and descriptions of complex inclusion/exclusion criteria should not be a requirement of this data bank. In addition, the proprietary nature of certain components of a clinical protocol (e.g., endpoints, size of trial and statistics, comparator agent, etc.) may constitute a competitive asset differentiating sponsors. Disclosure of such details in a public data bank would not advance the public access to clinical trials, and may be a deterrent to the research and development process.

The list of data elements is somewhat general and will be subject to sponsor interpretation. We assume the implementation plan that will be issued later in 2000 will address more specifically the type of information that will be required for inclusion in the data bank. One example would be that the information listed for "Contact" could be just the telephone number for the clinical trial site. Some site managers may not want to be named in a public data bank.

B. Time Requirements

According to the draft guidance, sponsors should submit protocol information..."(1) no later than 21 days after the trial is first opened for enrollment, (2) upon amending the protocol with respect to one of the required

data elements, or (3) when recruitment for the study is interrupted, resumed, or completed." The implementation plan should provide additional guidance on a reasonable timeframe for sponsor updates to the data bank, particularly with regard to instances (2) and (3), which can be expected to be recurring throughout a clinical trial. For example, current FDA regulations pertaining to IND protocol amendments allow information to be grouped and submitted at 30-day intervals (e.g, 21 CFR §312.30(e) allows information about investigators to be "grouped and submitted at 30-day intervals," and sponsors are encouraged to include reporting of multiple changes in single submissions). Accrual rates for clinical trials vary, but a timeframe should be considered that will allow meaningful information updates without adding undue administrative burden to NIH or sponsors.

Burden Estimate. On a related topic regarding the burden estimate required under the Paperwork Reduction Act, the *Federal Register* notice indicates that FDA anticipates original protocols will be updated 2.5 times per year (see 65 Fed. Reg. p. 16622, and top p. 16623). In response to FDA's request for comment on the accuracy of this estimate, as well as ways to minimize the burden of the collection of this data on those sponsoring clinical trials, we are convinced that FDA has greatly underestimated the burden of the collection of information. If one considers multicenter studies, we believe it is more likely to be at least 10 updates per protocol. Also, the estimated 5.6 hours on average per response does not account for the quality control review of the data before it is submitted to the data bank. We believe a more realistic figure would be 9 hours per response. While FDA calculates 77,084 hours spent per year, we believe it will be more like 495,540 hours per year (55,060 responses x 9 hours = 495,540 response-hours/year). Moreover, these burden estimates are conservative, depending on the data elements and other details that might be proposed in the forthcoming draft implementation plan. Reasonable accommodation of comments outlined above regarding Data Requirements and Time Requirements will help minimize the ongoing burden of collecting data.

VI. Identification of Trials Required to be Included in the Clinical Trials Data Bank

As we previously noted in 1998, Phase 4 (post-approval) trials should not be required for inclusion in the data bank because patient awareness of and access to the medicine has already been achieved. Also, clinical trials conducted outside of the US, and foreign sites of US clinical trials should not be required for listing. The inclusion of ex-US sites in the data bank would greatly increase the workload for the sponsor without providing significant benefit to the American public. Such information could be listed voluntarily by sponsors, at their option.

This section of the draft guidance refers to "group C protocols". Not all readers of this guidance are familiar with that terminology. It would be helpful to define the term(s).

General Comments

As the data bank is phased-in and experience is developed, NIH and FDA should be prepared to revise specific elements that prove not to be reasonably beneficial for patients and that may entail an undue reporting burden.

We are aware that NIH is developing methods to accept the information electronically as well as through receipt of paper. We would like to continue working with NIH/FDA to build on the work already accomplished between industry and FDA regarding electronic transfer of information.

Sincerely Yours,

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